PATENT SPECIFICATION

(11) **1 584 788**

(54) ION-SELECTIVE ELECTRODE

(71)   We, EASTMAN KODAK COMPANY, a Company organized under the Laws of the State of New Jersey, United States of America of 343 State Street, Rochester, New York 14650, United States of America do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to analytical measurement and in particular to ion-selective electrodes for determining specific ion concentrations in solution.

A great variety of electrode types and structures are known for the measurement of various ions in solution. Typically, devices for obtaining such measurements include a reference electrode and a separate ion-selective electrode. The ion selective electrode incorporates a reference cell. When simultaneously immersed into the same body of solution to be analyzed, the reference and ion-selective electrodes constitute an electrochemical cell, across which a potential develops. This potential is proportional to the logarithm of the activity of the ion of choice which is related to concentration in the solution of the ion of choice to which the ion-selective electrode is sensitive. The foregoing relationship between the potential and ionic activity in solution is described by the well-known Nernst equation. An electrometric device, usually either a direct reading circuit or a null-balance potentiometric circuit, is employed for measuring the potential between the electrodes.

In the past, the ion-sensitive electrode generally comprised an electrode body (usually some type of glass container) containing a known reference solution in contact with a half-cell of known potential, generally Ag/AgCl/"XMCl" and an ion-selective glass membrane mounted in an aperture in the electrode body in such a fashion that when the electrode was immersed in the unknown solution, the glass membrane contacted both the reference solution within the electrode body and the unknown solution. An appropriate metal probe coated with a layer of an insoluble salt of the metal immersed in the contained reference solution served as the contact for the electrode. The selectivity of the electrode was determined by the composition or components of the glass membrane. Such electrodes are referred to herein as "barrel" electrodes. U.S. Patent Nos. 3,598,713 and 3,502,560 provide detailed descriptions of electrodes of this type

According to the present invention, there is provided an ion-selective electrode comprising an internal reference electrode in dried form as hereinafter defined in contact with a hydrophobic dry-operative as hereinafter defined ion-selective membrane containing a binder and an ion-carrier, the regions of the membrane adapted to be in contact with analyte having a predetermined uniform thickness.

The ion-selective electrodes described herein require no preconditioning prior to use in an ion-sensing operation.

The reference electrode may comprise either a metal/metal-salt reference half-cell or a dried single- or multiple-layer redox couple reference electrode which is similarly wetted upon application of an aqueous sample as described hereinafter. The term "dried" as used herein is defined below.

According to a further preferred embodiment, the hydrophobic membrane includes an inert ion carrier dissolved in a suitable carrier solvent dispersed in a hydrophobic binder. A most preferred embodiment provides for electrodes of the type described which provide a substantially planar surface for contacting with a sample for testing and comprise a hydrophobic membrane of predetermined uniform thickness in regions intended for contact with a sample for analysis. The electrode optionally includes a support. A technique for making measurements of ion concentration by reading the electrode prior to substantial hydration thereof is also described.

The ion-selective electrode of the present invention, which is designed for use in the potentiometric analysis of liquids, is simple in structure, easily manufactured at a reasonable cost and therefore disposable, and highly accurate owing to its economically feasible single-use capability which insures the integrity of the ion-selective membrane for each new measurement. As will be described in somewhat greater detail below, the electrode can be prepared in a variety of formats and geometries.

For a complete understanding of the invention described herein it is necessary to have an understanding of the phenomenon of electrode drift.

Electrode drift is the variation in the potential sensed by an ion-selective electrode in contact with an ion-containing solution over a period of time.

Electrode drift is apparently due to a number of factors such as permeation of the ion-selective membrane by test solution solvent (generally water) with the passage of time, variations in ion concentration in the test solution in the region of the solution proximate the electrode, which variation is caused by the aforementioned solvent permeation.

All ion-selective electrodes demonstrate some drift, however, the phenomenon is minimized in conventional electrodes by preconditioning the electrode to bring it to an equilibrium state approximating that expected to be encountered in a testing situation. In this fashion the user diminishes the factors which cause drift and consequently reduces drift in the testing situation. One might expect, therefore, that the use of a totally "unconditioned" ion-selective electrode would result in severe drift of potentially catastrophic proportions which would prohibit such use of the ion-selective electrode until the equilibrium state usually achieved by preconditioning had been reached in the test situation. It has now been found that ion-selective electrodes can be prepared which can be used without preconditoning of any sort and that the drift exhibited by these electrodes, although sometimes substantial, can be calibrated to provide accurate and reproducible determinations of the concentration of specific ions in test solutions.

As used herein, the term "dry-operative" describes an ion-selective electrode which provides reproducible potentiometric determination of ionic activity which can be related to the ion concentration of aqueous test solutions with no requirement for "wet" storage (i.e., keeping in an aqueous solution) or preconditioning (i.e., soaking in a salt solution) prior to use. Essentially, what this means is that a "dry-operative" electrode produces accurate, reproducible and detectable determinations of potential which can be calibrated and thereby related via ionic activity to ionic concentration in an aqueous test solution without having first to be substantially hydrated or brought to the aforementioned equilibrium state. Many of the electrodes described herein perform in this manner even when used immediately after storage at RH 20%. The practical application of this definition will be made more apparent from the discussion and examples which follow.

The term "thin" when used in reference to individual layers of preferred embodiments of the electrodes of the present invention describes individual electrode layers having a maximum thickness of about 1.25 mm. Preferably, such "thin" layers are of the order of less than 0.25 mm in thickness. Most preferred are layers on the order of less than 0.05 mm.

The term "predetermined uniform" when used herein in reference to the thickness of the ion-selective membrane of a "dry-operative" electrode describes a thickness tolerance in regions of the layer intended for contact with a sample for

1,584,788

analysis. This tolerance is met if the drift exhibited by the electrode incorporating such a layer can be calibrated, i.e., can provide reproducible and detectable determinations of potential related to concentration by calibration within an error tolerance acceptable for the particular measurement without preconditioning or permitting the electrode to reside in the test solution for a period sufficient to achieve conditioning by the test solution. Electrodes which do not possess "predetermined uniform" thicknesses will exhibit a random drift which cannot be calibrated to provide results which are directly related to ionic concentration. Uniformity of thickness as exhibited by dry operativeness will generally call for a maximum variation in the thickness of the membrane of at most 20% in regions thereof intended for contact with a sample for analysis.

The term "dried" when used in reference to layers of electrodes described herein refers to physical state of such layers brought about by subjecting, in manufacture, the layer to drying conditions, i.e., conditions of temperature, reduced vapour pressure, etc., adequate to accomplish removal of sufficient solvent or dispersing medium as to render the layer non-tacky, as this term is commonly interpreted in the coating arts, prior to the application of any overlying layer(s). This drying to drive off solvent or dispersing medium is a major factor imparting the "dry-operative" capability to the electrodes of the present invention. Although the mechanism of this phenomenon is not fully understood, and applicants do not wish to be bound by any theory of operation for their electrodes, it appears that the shrinking which the "dried" layer undergoes with loss of liquid in drying assures intimate contact between the "dried" layer and the contiguous superposed ion-selective membrane even under relatively harsh storage conditions of very low relative humidity, i.e., 20% RH or less. In this regard, it is generally desirable to relate the relative humidity of drying conditions in manufacture to the expected conditions of use as this will provide an optimized state of hydration for the ion-selective electrode. This relation is, however, not necessary to obtain useful electrodes. More specific conditions and requirements for certain dried layers of the electrodes of this invention will be stated hereinafter.

Typical of the "dried" layers described herein are those obtained by forming layers under the following conditions:

(A) A solution comprising from 5 to 9% by weight gelatin is coated at a level of 64 g/m² and dried under the following conditions:

    (1) chill set for six minutes at 55°C and a dew point of 50% RH; and
    (2) dry for four minutes at 21°C and 50% RH;

(B) Solutions of from 5 to 9% of polyvinyl alcohol and poly(2-hydroxyethylacrylate) are coated at a level of about 64 g/m² and dried under the following conditions:

    (1) heat set for six minutes at 40°C and 50% RH; and
    (2) dried for four minutes at 35°C and 50% RH.

These drying conditions are not essential to obtain layers of the type described herein, however, they are typical of conditions which may be used to obtain dried layers of the type described herein using a variety of polymer matrixes suitable as the binder for the reference electrolyte layer. Such layers demonstrate the "dryness' required of the reference electrode layer prior to application of the ion-selective membrane.

The electrodes described herein are generally capable of producing concentration determinations which demonstrate a coefficient of variation of less than about 10%. Electrodes prepared in accordance with preferred embodiments hereof demonstrate coefficients of variation of less than 3% and in certain highly preferred embodiments, coefficients of variation of below 2% have been achieved. The coefficient of variation is the standard deviation divided by the mean and multiplied by 100. The "mean" is the average value of a series of numbers, i.e. the sum of the values divided by the number of values. Standard deviation is the number obtained by determining the deviations of each value in a series from the mean, squaring the deviations, summing the squared deviations, dividing by the number of values in the series and taking the square root of the result.

As described hereinabove, previous so-called "solid-state" electrodes required the incorporation as an internal electrolyte of either an aqueous salt solution, a hydrated salt, or a layer of salt impregnated glass to achieve operative measurements of ionic concentration. All such electrodes require preconditioning prior to use in an ion-sensing operation. It has now surprisingly been discovered that electrodes having a "dried" internal electrolyte and ion-selective membrane of predetermined uniform thickness can be used to achieve stable levels of precision

and accuracy in potentiometric ionic determinations similar to those until now achievable with electrodes which required preconditioning, at ambient conditions without any substantial preconditioning or wet storage. The ion-selective electrodes of the present invention present a dry solid appearance and require only a drop (i.e., below about 50 μl and preferably 10 μl) of solution to produce an accurate measurement. They require no preconditioning prior to use, measurements can generally be made in less than five minutes and because of their low cost they can be discarded after a single measurement, thereby avoiding contamination due to prior use thereby insuring integrity of the ion-selective membrane for each new measurement. Furthermore, a novel technique for using the ion-selective electrodes of this invention permits rapid yet accurate quantitative ionic determinations.

Although the layers described hereinafter are generally referred to as being "coated" one over another, it should be understood that the term "coating" is meant to include laminating or otherwise depositing the various strata one over another, as well as actually coating using conventional coating, dipping or extrusion techniques to achieve layering of the various strata.

The dry-operative ion-selective electrodes of the present invention comprise:

(a) a dried, internal reference element,

(b) in contact with the reference electrode, a hydrophobic ion-selective membrane (of predetermined uniform thickness in areas thereof intended for contact with a test solution), and

(c) an optional support.

Reference Electrode

As with any ion-selective electrode useful in the determination of ionic activity and consequently ionic concentration in solution, the electrodes of the present invention have an internal reference electrode which exhibits a fixed reference potential against which the potential occurring at the interface between the ion-selective electrode and the solution under test is measured.

According to the present invention, the reference electrode may be of two distinct types, both of which exhibit the required fixed potential necessary to achieve useful results. The useful reference electrodes are:

(1) metal/metal-salt electrodes (see Figure 1), and

(2) redox couple electrodes (see Figure 2).

Metal/Metal-Salt Electrodes

A commonly used internal reference electrode comprises a metal in contact with an insoluble salt of the metal which is in turn in contact with an electrolyte, i.e., a solution containing the anion of the salt. A very commonly used example of such an element is represented as $Ag/AgCl/"XMCl^-"$ ($XMCl^-$ indicating a solution of known Cl^- concentration) and comprises a silver wire having a coating of silver chloride applied thereto dipping into an aqueous solution of known chloride concentration. A calomel electrode, $Hg/Hg_2Cl_2/Cl^-$, is another example of this type of electrode. This type of internal reference electrode is used in most barrel electrodes and in the known, so-called "solid-state" electrodes. In known "solid-state" electrodes, the electrolyte solution comprises a hydrated gel, hydrated PVA or hydrophobic ion-exchange resin, as described above. The reference electrodes of the present invention are dried during manufacture and, unexpectedly, do not require conditioning prior to use.

According to the present invention, the metal/metal-salt reference electrode comprises a conductive layer of a metal in conducting contact with a layer of a salt of the metal as used in known electrodes and a dried electrolyte layer in contact with the metal-salt layer.

The conductive metal layer may comprise any suitable conductive metal of the well known types which have been used in such electrodes, and which is compatible with the structure, particularly the formats described herein. Particularly useful conductive metal layers include suitably thin layers of silver, nickel, platinum and gold.

The salt layer in contact with the conductive layer may comprise substantially any insoluble salt of the metal of the conductive layer which establishes a fixed interfacial potential with the metal of the conductive layer. Such layers, which are well known, generally comprise a salt of the metal which is a product of the oxidation of the metal, as, for example, $AgCl$ and Hg_2Cl_2. A highly preferred embodiment of the present invention uses the aforementioned well known

Ag/Ag_nX (wherein $X=S^=$, Cl^-, Br^- or I^- and n=1 or 2) interface to establish the potential of the reference electrode. Electrode elements of this type can be prepared using a number of well known techniques which include, by way of example, dipping a layer of silver as a wire, foil or supported thin layer into molten silver halide. According to a preferred embodiment of the present invention, the silver-silver halide couple is produced by vacuum depositing silver on a suitable support of the type described below, preferably an insulating film, and then chemically converting a surface stratum of the silver layer to silver halide. Generally, techniques for chemically converting metal to metal halide involve exposure or contact of the surface of the metal, in this case silver, with a solution of a salt of the halide to be formed for a period and at a temperature sufficient to cause the desired conversion. Typical conditions for this sort of chemical conversion are well known, and examples of simple and preferred techniques are shown in the examples below. Other useful techniques for preparing such electrodes are described in U.S. Patent Nos. 3,591,482; 3,502,560 and 3,806,439. Although the teachings of all of these references are directed primarily to the preparation of wire electrodes, the application of ordinary engineering skill will render their application to the manufacture of electrodes constructed on thin films of polymeric support apparent. Alternatively, a discrete layer of silver halide may be coated over the silver layer so long as appropriate contact between the silver and silver halide is maintained.

Although it is possible to obtain the metal/metal-salt interface with substantially any ratio of metal layer to salt layer thickness, in a preferred embodiment which assures a sufficiently dense layer of metal salt it is preferred that the insoluble metal-salt layer have a thickness equal to at least 10% of the overall thickness of the conductive metal layer. According to a preferred embodiment of the present invention wherein a surface layer of a vacuum-deposited silver layer is converted to a suitable salt, from 10 to 20% of the thickness of the silver layer is converted to silver salt using chemical conversion techniques.

The second member of the metal/metal-salt reference electrodes of the present invention comprises the electrolyte layer. According to a preferred embodiment of the present invention, the electrolyte layer is a dried hydrophilic layer.

The dried electrolyte solution of the present invention comprises a hydrophilic binder having a salt in solid solution therewith. According to a preferred embodiment, the anion of this salt is common to the anion of the salt of the metal-salt layer and at least a portion of the cation of said salt is identical to the ion which the electode is designed to detect.

"Dried" hydrophilic electrolyte solutions as described herein are specifically distinguished from the hydrated polyvinyl alcohol layers described in U.S. Patent No. 3,856,649. The "dried" reference solution of this invention comprises the *dried* residue of a solution of a salt and a suitable hydrophilic polymeric binder in a solvent for the polymer and the salt. This distinction will be made more apparent by the discussions of making and using the electrodes of the instant invention which are presented hereinafter.

The binder for the "dried" reference electrolyte solution may comprise any hydrophilic material suitable for the formation of continuous, coherent, cohesive layers compatible with the salt of the electrolyte layer and, if formed by coating, a solvent sytem for both the ionic salt and the polymeric binder. Preferred materials of this type are hydrophilic natural and synthetic polymeric film-forming materials such as polyvinyl alcohol, gelatin, agarose, deionized gelatin, polyacrylamide, polyvinyl pyrrolidone, hydroxyethyl acrylate, hydroxyethyl methacrylate and polyacrylic acid. Specifically preferred from among these materials are the hydrophilic colloids such as gelatin (especially deionized gelatin), agarose, polyvinyl alcohol and hydroxyethyl acrylate.

Some residual solvent for the ionic salt must remain in the "dried solution" to permit electrolytic conductivity within the polymeric layer. Thus, the layer must not be so thoroughly dried as to remove all residual solvent. As a general rule, when water is the solvent, the residual water comprises less than about 20% preferably from greater than zero to 20% and more preferably from 1 to 2% of the total weight of the "dried solution" and the "dried" electrolyte layer is non-tacky. Similar residual solvent levels are desirable with solvents other than water.

The ionic salt which is dissolved in the polymeric binder solution will be determined by the composition of the metal/metal-salt portion thereof. For example, in a potassium selective electrode which uses silver chloride as the

insoluble metal salt, potassium chloride is a logical choice although sodium chloride, may also be used. For sodium ion determinations in a similar configuration, sodium chloride would be useful. Thus, the salt will generally be a water-soluble salt having a cation selected from ammonium, alkali metals and alkaline earth metals, mixtures of same or any other suitable cation to which the electrode responds, and as anion a halogen or sulphur depending upon the composition of the metal-salt layer. Conductive metal salts of these anions are commonly insoluble in water.

Appropriate solvents for the polymeric binder and ionic salt will depend largely on the nature of the polymer and the salt. Generally, polar solvents suitable for dissolving the salt and the polymer are satisfactory. Thus, water is a preferred solvent for layers of hydrophilic materials such as polyvinyl alcohol and gelatin.

Since the thickness of the "dried" electrolyte layer will to some extent determine the response characteristics of the electrode, it is generally desirable to maintain the "dried" layer rather thin. Layers having dry thicknesses of the order of from 0.0025 mm to 0.013 mm have been found useful. A preferred thickness is 0.005 mm. Of course, where electrode response characteristics are not critical, the thickness of the layer may vary over a wide range and only the application of sound engineering skills and the use requirements of the finished electrode will determine its limits.

The concentration of ionic salt in the "dried electrolyte layer" may also be varied widely, depending upon response time desired, etc. and especially the level or amount of polymer used. In the preferred embodiments described herein wherein the binder level ranges from 2.4 g/m^2 to 10 g/m^2, the concentration of the salt ranges from 1.40 to 2.5 g/m^2. Below this level, electrode drift may be a problem as elaborated below, and above this level coating of the layer becomes somewhat difficult. Of course, where drift is not critical, layers of substantially greater thickness are used, or where layers are prepared by some technique other than coating, concentrations of salt outside these ranges may be similarly useful. Generally, salt concentrations of from 30 to 50 percent by weight total solids in the layer are preferred.

When the reference electrode is prepared by coating the various layers one over another, it may be desirable to include surfactants or coating aids in the coating solution during manufacture. Such materials should generally be nonionic and, whatever their composition, they should not include ions which introduce variants into the fixed potential differences existing at the various electrode layer interfaces and are most preferably potentiometrically inert. Of course, where additives which do introduce variants into the potentials exhibited at the various interfaces are used, it is possible to compensate for these using a differential mode of measurement which compares the readings of two identical ion-selective electrodes, one of which is contacted with a solution of known ion concentration and the other of which contacts the unknown test solution. Among the materials found useful for this purpose are natural surfactants such as saponin and synthetic materials such as poly(ethylene glycol) and a material commercially available from Olin Mathieson Company under the tradename "Surfactant" 10G. Other useful materials of this type include octyl phenoxy polyethoxy ethanols such as TX-100, TX-405, commercially available from Rohm & Haas Company.

In an alternative embodiment useful metal/metal-salt (specifically Ag/AgX) reference electrode elements can be prepared using techniques common to the manufacture of photographic film.

According to such procedures either or both of the metal (i.e. silver) and metal salt (i.e. silver halide) are prepared by coating suitable silver halide photographic emulsions and processing as required. For example, a useful silver halide layer can be prepared by applying to a vacuum deposited silver layer, by coating a conventional fine grain silver chloride-gelatin emulsion at coverages of from 0.054 to 0.54 g/m^2 of gelatin and 1.16 to 1.83 g/m^2 of silver as silver chloride. In evaluations with standard chloride solutions, such electrodes demonstrated substantially Nernstian response (i.e. slopes of 59 mv/decade.)
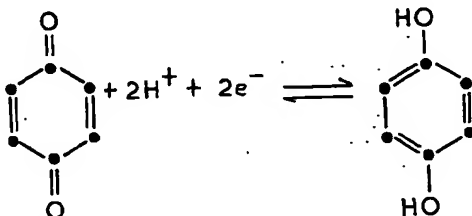
Useful silver layers which can be overcoated with silver halide layers as just described have been prepared by coating a poly(ethylene terephthalate) support with a layer of fine grain silver chloride, gelatin emulsion at a coverage of 2.02 g/m^2 of silver as silver chloride and 95 mg/m^2 of gelatin using conventional photographic film manufacturing techniques. The silver chloride layer was then developed for five minutes in a standard black and white developer solution known as "Kodak" Developer D-19 at room temperature and under white light conditions. "Kodak" is

a registered Trade Mark. After thorough washing and drying this layer was overcoated with a silver chloride emulsion as just described. Samples of this electrode responded acceptably to standard chloride ion solutions.
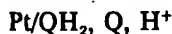
Useful electrodes have also been obtained by coating the silver chloride emulsion over evaporated layers of gold, copper and nickel and using fine grain silver bromide emulsions to prepare the metal salt layer.

Oxidation-Reduction Electrodes

The second type of internal reference electrode useful in the successful practice of the present invention is the so-called oxidation-reduction electrode (hereinafter redox electrode). Redox electrodes have been described and generally include an inert metal wire dipping into a solution containing two different oxidation states of a chemical species. An example of such an electrode comprises a platinum wire dipping into a solution containing ferrous and ferric ions. Such a cell is abbreviated $Pt/Fe^{++}, Fe^{+++}$. The electrode reaction is $Fe^{+++}+e^-\rightleftharpoons Fe^{++}$. Redox electrodes can also be made with organic molecules that can exist in two different oxidation states. The most widely used of this type is the so-called quinhydrone electrode in which the redox system is:

and the cell is represented as:

$$Pt/QH_2, Q, H^+$$

Redox electrodes of this type can also be prepared in a "solid-state" format to provide the internal reference element of the composite ion-selective electrodes of the present invention. Alternatively, such electrodes may be used as external reference electrodes in the overall determination of ion concentrations in solution in place of conventional external reference electrodes such as the saturated calomel (i.e., $Hg/HgCl_2$) electrode. U.S. Patent No. 3,730,868 also describes such a redox electrode.

The redox electrode of the present invention comprises:
(a) a solid, electrically conductive layer in contact with
(b) a redox couple.

The redox couple may be dissolved or dispersed in the electrically conductive layer or be provided as a discrete solid layer comprising the redox couple dissolved or dispersed in a suitable binder and in conducting contact with the conductive layer.

The Conductive Layer

The conductive layer of the redox reference electrode comprises an electrically conductive material or conductor (as this term is conventionally understood in the art). It will be appreciated that the conductive material should not interact with the redox composition except in the desired and controlled electrochemical fashion required for operation of the electrode, i.e., to establish a stable reference potential. Useful results have been obtained with such inert conductors as carbon, platinum, gold and nickel. So long as the conductor is selected so that no unstable electrochemical or other undesired interaction with the redox couple is observed, the choice is not critical. A particularly useful conductor is carbon (in particular, particulate carbon), as will be shown in the examples and described in greater detail below.

In certain embodiments, as in the case of carbon where the inert conductor may be in the form of discrete conductive particles, it may be necessary that such particles be maintained in electrically conductive contact in a solid layer by means of some binder or matrix. The binder may comprise any material which permits intimate particle-to-particle contact and conductive contact between the

conductor and the redox couple as described hereinafter. Generally, such binders comprise relatively low concentrations of hydrophilic polymers such as gelatin, polyvinyl alcohol and polyvinyl pyrrolidone. It is, however, possible to use hydrophobic polymers such as silicone rubber for the binder. Whatever the binder used, the ratio of conductor to binder must be sufficiently high that the resistance of the layer is low enough to insure adequate electrical conductivity. Such resistances are obtainable with weight ratios of conductor to binder of between about 1:1 and about 3:2.

The Redox Couple Composition:

The redox couple composition comprises the soluble redox couple and whatever other means are required to maintain the composition in a solid form until such time as the electrode is wetted and at least some portion of the redox couple is dissolved and contacts the conductor. This other means generally comprises a matrix or binder of one sort or another which contains the redox couple as a solid solution or dispersion.

The redox couples of the present invention, as alluded to above, comprise pairs of the same chemical species (usually ions) in differing oxidation states.

The formal potential of the reference electrode of the present invention, i.e., the electrical potential of the redox couple at equal concentrations of its reduced and oxidized components at some defined finite value of ionic strength, is determined by:

(1) the redox couple chosen and

(2) the ratio of activities of oxidized to reduced components.

According to a preferred embodiment of the present invention, the ratio of the oxidized to the reduced component (i.e., the molar ratio of material in one oxidation state to material in the other oxidation state) is about unity (1), since the redox buffer capacity is largest at this ratio. Of course, depending upon the type of measurement to be made using the electrodes described herein, this ratio may be varied quite broadly.

When the electrode is wetted with a sample solution, the redox couple must be capable of establishing a stable interface with the conductive layer to establish a stable and reproducible potential; i.e., the redox couple must be capable of exchanging electrons with the conductive layer in a constant fashion when the potentiometric circuit is completed. It is important that the conductive layer and the redox couple together poise the potential of the redox chemistry in a fast· electrochemical exchange reaction between the redox couple and the conductor. It is this capability to establish a constant potential which is referred to herein as the "compatibility" of the redox couple with the conductive layer. A redox couple which readily establishes such a fixed potential with a given conductor is said to be "compatible" therewith.

According to a preferred embodiment, it is, of course, desirable that in order for the electrode to possess an extended shelf-life capability, the oxidized and reduced forms of the couple should be stable for the desired shelf-life.

Redox couples which have been found particularly useful in the successful practice of the present invention include ferric/ferrous ion couples such as $Fe(CN)_6^{-3}/Fe(CN)_6^{-4}$ and cobaltic/cobaltous couples such as $Co(terpyridyl)_2^{+3}/Co(terpyridyl)_2^{+2}$ wherein terpyridyl is 2,6-di-2'-pyridylpyridine.

Any redox couple capable of exchanging electrons with a compatible conductive layer and sufficiently stable against aerial oxidation as to provide a useful shelf-life is useful in the successful practice of the invention.

Although some redox couples may be applied as a solid layer directly to the conductive layer without a matrix or binder, in view of the high solubility of many of the useful redox couples and the difficulty with which materials of this type are applied to the conductive layer in their solid form (i.e., as crystals, etc.), it is generally desirable to apply the redox couple as a dispersion or solution in a suitably porous or water permeable binder or matrix.

The preferred water permeable matrixes for the redox couple comprise a hydrophilic colloid such as gelatin, polyvinyl alcohol, polyacrylamide and polyvinyl pyrrolidone, which colloid is most preferably:

(a) sufficiently hardened or cross-linked to prevent substantial dissolution thereof by water which may contact it, and

(b) sufficiently hydrophilic to permit electroytic contact with the conductive metal layer.

As alluded to hereinabove, it is also possible to use highly porous layers of

hydrophobic material wettable by virtue of their porosity and permitting conducting contact between particulate members of the redox couple also by reason of this porosity. Thus, water permeable, highly porous layers (i.e., comprising over about 60% and preferably over about 75% void volume) of such hydrophobic materials as cellulose acetate or 85/10/5 poly(n-butylmethacrylate-co-2-acrylamido-2-methylpropane sulphonic acid-co-2-acetoacetoxyethyl methacrylate) can be used as the binder or matrix for the redox couple.

Although the redox reference electrodes are generally prepared in a two-layer configuration (i.e., a solid layer of inert conductor in conducting contact with a superimposed solid dried redox couple layer), it has also been found that both the inert conductor and the redox couple may be incorporated into a single layer to provide a useful electrode. In this configuration, it is preferred to use a hydrophilic matrix of the type described above in connection with the redox couple layer for the combined layer; however, hydrophobic binders are also useful. Embodiments of single-layer reference electrodes are described in the Examples below. The techniques for their preparation and use are identical to those of the two-layer or double-layer electrodes described herein.

Ion-Selective Membrane

Whichever of the foregoing internal reference electrodes is used, the ion-selective membrane is laminated, coated or otherwise applied directly thereover. It is important to the successful practice of the present invention that the ion-selective membrane be applied at the time of manufacture so as to assure intimate and uniform contact with the surface of the reference electrode contiguous with the ion-selective membrane at least in those areas intended for contact with a test solution to obtain a "dry-operative" electrode. Such intimate uniform contact of the ion-selective membrane with the dried internal reference electrode at the time of manufacture produces a reference electrode-ion-selective membrane interface which will respond almost immediately upon contact of the ion-selective membrane with a test solution.

Among the patents and publications which describe ion-selective membranes of the type useful in the instant invention are: U.S. Patents No. 3,562,129; 3,753,887 and 3,856,649, United Kingdom Patent No. 1,375,446; German OLS 2,251,287 and the articles by Morf, W. E., Kohr, G., and Simon W., Reduction of the Anion Interference in Neutral Carrier Liquid-Membrane Electrodes Responsive to Cations", *Analytical Letters*, Vol. 7, No. 1, pp. 9—22 (1974);

Morf, W. E., Ammann, D., Pretsch, E., and Simon, W., "Carrier Antibiotics and Model Compounds as Components of Ion-Sensitive Electrodes", *Pure and Applied Chemistry*, Vol. 36, No. 4, pp. 421—39 (1973);

Ammann, D., Presch, E., and Simon, W., "Sodium Ion-Selective Electrode Based on a Neutral Carrier", *Analytical Letters*, Vol. 7, No. 1, pp. 23—32 (1974);

Cattrall, R. W., and Freiser, H., *Anal. Chem.*, 43, 1905 (1971); and

James, H., Carmack G., and Freiser, H., *Anal. Chem.*, 44, 856 (1972).

Membranes of this type which are well-known generally include an inert hydrophobic binder or matrix having dispersed therein an ion carrier which imparts selectivity to the membrane, dissolved in a carrier solvent to provide adequate ion mobility in the membrane. The carrier solvent generally also serves as a plasticizer for the membrane binder.

Binders for use in the ion-selective membrane of the instant invention include any of the hydrophobic natural or synthetic polymers capable of forming thin films of sufficient permeability to produce, in combination with the ionophores and ionophore solvent(s), apparent ionic mobility thereacross. Specifically, polyvinyl chloride, polyvinylidene chloride, polyacrylonitrile, polyurethanes (particularly aromatic polyurethanes), copolymers of vinyl chloride and vinylidene chloride, polyvinyl butyral, polyvinyl formal, polyvinylacetate, silicone elastomers and copolymers of polyvinyl alcohol, cellulose esters, polycarbonates, carboxylated polymers of vinyl chloride and mixtures and copolymers of such materials have been found useful. Films of such materials which include the ion carriers and carrier solvents may be prepared using conventional film coating or casting techniques and, as shown in the examples below, may be formed either by coating and film formation directly over the internal reference electrode or some suitable interlayer or by formation separately and lamination thereto.

The ion carrier used in the ion-selective membrane is generally a substance capable of selectively associating or binding to itself preferentially a desired specific alkali metal, alkaline earth, ammonium or other ions. The manner in which the ion

becomes associated with the carrier is not fully understood, but it is generally thought to be a steric trapping phenomenon complexing by coordination or ion exchange. Suitable ion carriers are more fully described below.
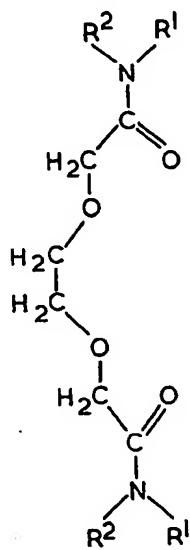
The selectivity of the electrode for a particular ion is due to the chemical nature of the ion carrier and, thus, the use of different chemical components as the uncharged ion carrier provides different membranes for use in ion-selective electrodes specific to different ions. Exemplary of such components are a large number of substances, some of them known to be antibiotics, which includes:

(1) valinomycin, a potassium-selective (over sodium), ion carrier that imparts to a membrane constructed in accordance with this invention a potassium ion selectivity of the order of 10^{-4}, and an ammonium ion selectivity (over sodium) of the order of 10^{-2};

(2) cyclic polyethers of various constitution which make the membrane selective to lithium, rubidium, potassium, caesium or sodium; and

(3) other substances having ion selectivity similar to valinomycin such as other substances of the valinomycin group, tetralactones, macrolide actins (monactin, nonactin, dinactin, trinactin), the enniatin group (enniatin A, B), cyclohexadepsipeptides, gramicidin, nigericin, dianemycin, nystatin, monensin, antamanide and alamethicin (cyclic polypeptides).
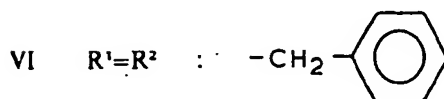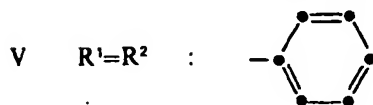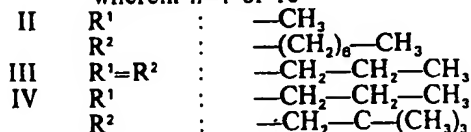
There can also be used either a single substance or mixtures of substances of the formula:
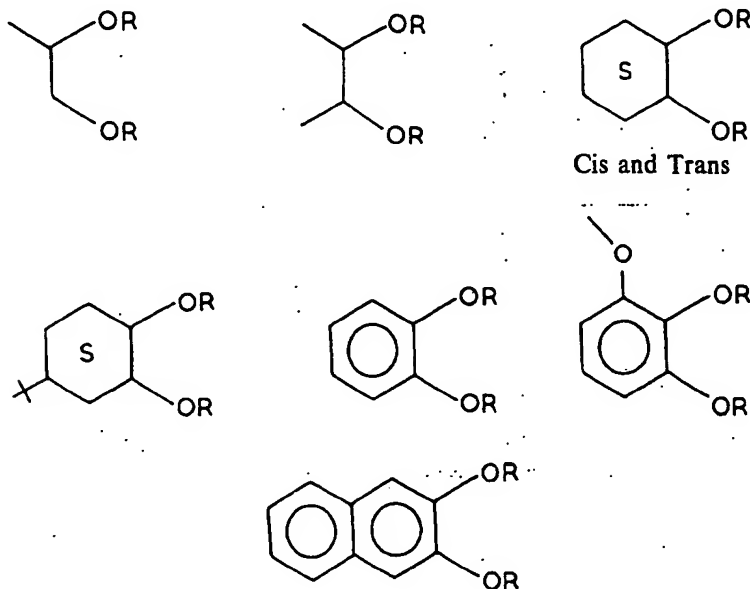

wherein:

I	R^1	:	$-CH_3$
	R^2	:	$-(CH_2)n-COO-CH_2-CH_3$

wherein n=1 or 10

II	R^1	:	$-CH_3$
	R^2	:	$-(CH_2)_6-CH_3$
III	$R^1=R^2$	:	$-CH_2-CH_2-CH_3$
IV	R^1	:	$-CH_2-CH_2-CH_3$
	R^2	:	$-CH_2-C-(CH_3)_3$

V	$R^1=R^2$	:	

VI	$R^1=R^2$	:	$-CH_2-$

Other useful ion carriers include tetraryl borates (especially tetraphenyl boron) and quaternary ammonium salts. Compounds such as trifluoroacetyl-p-alkyl benzenes are described in U.S. Patent No. 3,723,281 for carbonate ions HCO_3^-.

Compounds of the following structural formulas are also useful as ionophores:

Cis and Trans

wherein:
  a) $R=CH_2CON(CH_2CH_2CH_3)_2$
  b) $R=CH_2CON-(CH_2)_{11}-CO_2CH_2CH_3$
           |
           CH_3

These materials are described by Amman, D., Bissig, R., Güzzi, M., Pretsch, E., Simon W., Borowitz, I. J., Weiss, L., in Helv. Chim. Acta, 58, 1535 (1975).

Numerous other useful materials are described in the foregoing publications and patents, as well as other literature on this subject.

The concentration of ion carrier in the membrane will, of course, vary with the particular ion carrier used, the ion undergoing analysis and the carrier solvent. It has generally been found, however, that ion carrier concentrations of below 0.1 g/m^2 of membrane, assuming the membrane thicknesses preferred herein, result in marginal and generally undesirable responses. Ion carrier concentrations of between 0.3 and 0.5 g/m^2 are preferred. The ion carrier can be incorporated at levels much higher than this; however, because of the cost of many of these materials, use of such levels is not economically sound.

The carrier solvent provides ion mobility in the membrane and, although the ion-transfer mechanism within such membranes is not completely understood, the presence of a carrier solvent is apparently necessary to obtain good ion transfer.

The carrier solvent must, of course, be compatible with the membrane binder and be a solvent for the carrier. In the structure of the present invention, two other characteristics are most desirable. One is that the carrier solvent be sufficiently hydrophilic to permit rapid wetting of the membrane by an aqueous sample applied thereto to permit ionic mobility across the interface between the sample and the membrane. Alternatively, the carrier must be rendered hydrophilic by the action of a suitable noninterfering surfactant which improves contact between the sample in contact with the membrane and the carrier.

The other highly desirable characteristic is that the carrier solvent be sufficiently insoluble in water that it does not migrate significantly into an aqueous sample contacted with the surface of the membrane as described hereinafter. Generally, an upper solubility limit in water would be 4.0 g/l with a preferred limit lying below 1 g/l. Within these limits, substantially any solvent for the ion carrier which is also compatible with the binder may be used. As mentioned above, it is, of

1,584,788

course, preferred that the solvent also be a plasticizer for the binder. It is also desirable that the carrier solvent be substantially non-volatile to provide extended shelf-life for the electrode. Among the useful solvents are phthalates, sebacates, aromatic and aliphatic ethers and adipates. As shown in Example 8 below, specific useful carrier solvents include bromophenyl phenyl ether, 3-methoxyphenyl phenyl ether, 4-methoxyphenyl phenyl ether, dimethylphthalate, dibutylphthalate, dioctylphenylphosphonate, bis(2-ethylhexyl)phthalate, octyldiphenyl phosphate, tritolyl phosphate and dibutyl sebacate. Particularly preferred within this class is bromophenyl phenyl ether for potassium electrodes using valinomycin as the ion carrier. A large number of other useful solvents are specified in the references mentioned above which describe the preparation of ion-selective membranes and any of these which permit assembly of electrodes of the type described herein may be used in the successful practice of the present invention.

The concentration of carrier solvent in the membrane will also vary greatly with the components of a given membrane; however, weight ratios of carrier solvent to binder of between about 1:1 to about 5:2 provide useful membranes. The thickness of the membrane will affect electrode response as described in somewhat more detail below, and it is preferred to maintain the thickness of this layer below 0.125 mm and preferably 0.025 mm. As also described in greater detail below, the uniformity of thickness of the ion selective membrane plays an important role in the optimum utilization of electrodes of the type described herein. Thus, if maximum advantage in terms of storage capability and brevity of response time is to be obtained, the ion-selective membrane should be of relatively uniform thickness as defined above.

Support

According to preferred embodiments, the ion-selective electrodes of the present invention include a support which may be comprised of any material capable of bearing, either directly or by virtue of some intervening adhesion-improving layer, the other necessary portions of the electrode which are described in detail hereinafter. Thus, the support may comprise ceramic, wood, glass, metal, paper or cast, extruded or molded plastic or polymeric materials. The composition of the support is relatively unimportant, so long as it is capable of carrying the overlying electrode components and it is inert; i.e., it does not interfere with the indicating potentials observed as, for example, by reacting with one of the overlying materials in an uncontrolled fashion. In the case of porous materials such as wood, paper or ceramics, it may be desirable to seal the pores before applying the overlying electrode components. The means of providing such a sealing are well known and no further discussion is necessary here: Electrically insulating supports are preferred although, as described hereinafter, metallic conductive supports which serve multiple purposes are equally useful and may in fact simplify the structure of the electrode.

According to a highly preferred embodiment of the present invention, the support comprises a sheet or film of an insulating polymeric material. A variety of film-forming polymeric materials are well suited for this purpose, such as, for example, cellulose acetate, poly(ethylene terephthalate), polycarbonates and polystyrene. The polymeric support may be of any suitable thickness typically from 0.05 to 0.5 mm. Similarly thin layers or surfaces of other materials mentioned above could be used. Methods for the formation of such layers are well known in the art.

In certain cases, a separate and distinct support need not be provided. Such a case occurs when one or more layers of the electrode demonstrate sufficient mechanical strength to support the remaining portions of the electrode. For example, when a metal/insoluble metal-salt electrode is used as the internal reference electrode, the metal layer may be in the form of a self-supporting foil. The metal foil serves as the support, an integral portion of the internal reference electrode, as well as a contact for the electrode.

Preparation of the Electrode

The solid-state electrodes of the prior art are commonly manufactured using a conductive wire as the starting material and dipping the wire sequentially into generally highly viscous solutions of the components of the individual finished electrode layers to construct a bulbous multilayer "solid-state" electrode. See, for example, U.S. Patent No. 3,856,649. Alternatively, as shown in U.S. Patent No. 3,649,506, individual layers of ion-selective glass are applied over the tip of a conductive wire. In either of these situations, the resulting ion-selective membrane

is of relatively non-uniform thickness in those areas intended for contact with an aqueous solution whose ionic activity is to be determined.

Wire electrode configurations are within the scope of the present invention. However, when such electrodes are prepared, care must be exercised to reduce discrepancies in layer thickness (to within the tolerances described herein), which might provide undesirable results in the novel measuring methods described hereinafter.

Electrodes of the present invention are prepared by coating, laminating or otherwise applying the various individual layers one over another in any conventional fashion.

Thus, a typical manufacturing procedure for a metal/insoluble metal-salt reference element electrode would involve chemically converting or otherwise applying a layer of an insoluble metal salt to a layer of a compatible conductive metal in the form of a coating on a nonconductive substrate or a metallic foil, overcoating the metal-salt layer with an electrolyte solution layer, *drying* the thus applied layer to remove solvent (see definition of "dried" hereinabove), and *subsequently* overcoating with a solution of the components of the ion-selective membrane and drying to provide a complete electrode. Alternatively, the layers can be laminated so long as intimate contact between layers is achieved and maintained, and uniformity of thickness of the ion-selective membrane is attained.

The particular drying conditions which must be applied to the internal reference electrode in the manufacture of any specific ion-selective electrode will, of course, vary greatly depending upon the composition of the electrode layers, particularly the binder used, the solvent or dispersing medium used to form the layer and these can be readily determined by the skilled artisan. Typical conditions are described in the examples below for layers of the composition described therein.

Coating of the various electrode layers provides a uniquely simple yet efficient method for preparing electrodes as described herein. Using well known techniques, the various layers can be deposited under very carefully controlled conditions which provide highly accurate layer composition, degree of dryness and layer thickness, all of which are extremely important to the successful preparation of electrodes as described herein. Once prepared by coating, which will usually take place in a planar or substantially planar configuration, if the electrode has been prepared on pliant support, it may be fashioned into almost any useful geometry, by cutting or bending, which will permit contact of the ion-selective membrane with a test solution. As described below, a preferred technique for using the electrode is in a substantially planar configuration by the application of a drop (less than about 50 μl) of test solution to the ion-selective membrane.

The invention will now be described with reference to the accompanying drawings in which:—

Figure 1 is an isometric view of apparatus constructed in accordance with the invention;

Figure 2 is a sectional view taken along the section lines V—V of Figure 1; and

Figure 3 shows typical traces of potential vs. time obtained using the ion-selective electrodes of the present invention as described in Example 37.

In use, potentiometric analyses of liquids can be performed by mounting two of the aforedescribed electrodes in spaced relationship in a frame of the type depicted in Fig. 1. As shown, a frame 20 is in the form of a planar member 22 which, when used with automatic processing equipment, lends itself to easy stacking and storage. Two rectangular cavities are formed in the bottom surface 23 of the planar member 22 to receive and support in spaced parallel relationship two similarly shaped electrodes 24, 26, shown in phantom lines. The electrodes 24, 26 are identical in structure, having an upper, ion-selective, membrane below which lie layers forming either a metal/metal salt electrode or an oxidation-reduction electrode. The frame is fabricated of a non-conductive material, preferably plastic, to isolate the electrodes from each other electrically.

In the upper surface 30 of the planar member 22, apertures 32 and 34 are formed to enable leads 36 and 38 of an electrometer 40 to make electrical contact with the conductive layers of the electrodes 24 and 26, respectively. To facilitate electrical contact between the electrometer leads 36 and 38 and the conductive or metal layer of the electrodes 24 and 26, it is desirable that the upper layers of the electrodes (i.e. the ion-selective membrane, the reference electrolyte, and the insoluble metal-salt or the ion-selective membrane and the Redox couple layer be absent from the electrode structure in the vicinity of the apertures 32 and 34.

Also formed in the upper surface 30 of the member 22, are circular apertures A and B, one being positioned directly above each of the electrodes and communicating with the ion-selective membrane thereof. Through these apertures, single drops of a reference liquid and the test liquid make contact with the electrodes. To prevent spreading of the drop across the surface 30, apertures A and B are reamed to create a sloped surface at the boundary edge.

To enable ionic movement between the liquid drops positioned on apertures A and B, as is required in making potentiometric measurements, a "bridge" is provided between the apertures A and B, the bridge is in the form of a groove 42 formed in the surface 30 between the apertures A and B. Preferably, the groove 42 is coated with a surfactant capable of promoting ionic migration. Suitable surfactants include "Triton X-100", the registered Trade Mark of an octylphenoxy polyethoxy ethanol produced by Rohm & Haas, or "Olin 10G", the registered Trade Mark of a nonylphenoxy polyglycerol produced by Olin-Mathieson, if the plastic of the frame is hydrophobic. The drops will then flow together by reason of capillary action to create a junction. Alternatively, the groove 42 may be coated with an ion-porous material, comprising, for instance, a binder, a thickener, and a substance such as polycarbonate or polyamide mixed with atomized silica or glass powder.

Referring now to the cross-sectional view of Fig. 2, when a reference liquid drop 50 and a test liquid drop 51 are deposited on the apertures A and B, respectively, there is a tendency for the drops to spread over the ion-selective membrane of the electrodes 24, 26. If not curtailed, liquid from these drops will run down the edges of the electrodes, thereby short-circuiting the various layers. This will produce a faulty electrometer reading. To curtail such flow, endless annular grooves 52 are formed in the lower surface 23 of the planar member 22, such annular grooves surrounding the apertures A and B and being positioned within the electrode-receiving cavity. A platform 56 defined by an inner race 58 of the groove 52 is slightly recessed from the electrode surface (such as a distance of 0.25 mm). The effect of this structure is to produce a meniscus between the platform 56 and the ion-selective surface of the electrode, such meniscus acting to prevent further liquid flow toward the edges of the electrode due to surface tension effects. To provide an effective restraint to meniscus flow, it is preferable that the annular grooves 52 have a minimum width (w) of at least 0.025 cm, and that the edge 56 of the inner race be sharply defined. Alternatively, the annular grooves may be replaced with an annular strip of adhesive. A typical surface area for platform 56 for drop volumes of 10 microlitres is approximately 20 sq. millimetres, as typically is defined by a diameter of apertures A and B of approximately 2.0 mm, and by the inner diameter of the annular groove of approximately 5.0 mm.

Other additives such as dyes, plasticizers, etc., as desired may also be incorporated into the layer, so long as they do not interfere with the functions of the layer or components of the electrode.

Since the hydrophobic membrane layers described below are generally coated directly over the hydrophilic reference electrode, it is not entirely unexpected that, with certain embodiments of the electrodes described herein, adhesion problems between these two layers sometimes occur. In such instances, it may be useful to incorporate thin adhesion-improving or subbing layers between the reference electrode and the hydrophobic membrane. Care must, of course, be exercised to insure that such layer(s) do not interfere with the conductive contact between the membrane and the internal reference electrode and that no materials are introduced which might interfere with the fixed potential established by the reference.

It is important that the electrolyte layer be dried prior to application of the overlying ion-selective membrane if the electrode is to be dry operative. If the hydrophobic ion-selective membrane is applied over the reference electrode while it is still wet or fully hydrated as suggested in the prior art then, upon storage of the electrode at ambient conditions, the water present in the reference electrode will migrate out of the electrode. Since the electrolyte layer is hydrophilic, i.e., water swellable, upon evaporation therefrom the electrolyte layer apparently contracts while the overcoated hydrophobic membrane does not undergo any substantial contraction. Thus, the possibility exists for the occurrence of gaps or voids (i.e., reticulation) between the reference electrode and the hydrophobic membrane which will at least partially remove them from electrolytic contact until such time as the hydrophilic electrolyte solution is rehydrated and once again swells to a

point where contact between the internal reference electrode and the membrane is reestablished.

Electrodes using redox reference elements are prepared using techniques similar to those described above for the metal/insoluble metal-salt reference electrodes. Thus, the inert conductive layer, which may be a metal wire or foil or, alternatively, a dispersion of a particulate conductor such as carbon, is coated with a solution or dispersion of the redox species-containing layer, this latter layer dried and an ion selective membrane applied thereto as described above. Alternatively, the inert conductor and the redox species may both be incorporated into a matrix or binder composition and a single layer coated to provide the desired reference element. Of course, individual layers may be laminated in conducting contact to provide a similarly useful structure.

Use:

The ion selectivity of membrane electrodes can be observed by measuring the steady-state difference in electrical potential between solution 1 and solution 2 (both usually aqueous) in the cell arrangement schematically represented by the following:

Reference electrode 1/solution 1//membrane//solution 2/reference electrode 2

The calculations required to determine the ionic activity of solution 2 (generally the solution of unknown concentration) are derived from the well-known Nernst equation and are discussed in detail in a paper entitled "Cation Selectivity of Liquid Membrane, Electrodes Based upon New Organic Ligands" of Simon and Morf reported in the Pungor-edited reference cited above.

The electrode described herein incorporates within its structure substantially all of the components needed for making a potentiometric determination with the exception of a second reference electrode, the potential-indicating device and associated wiring so that in use the user merely needs to provide for contacting the sample with the ion-selective membrane, preferably by application of a small quantity of the sample to be analyzed (on the order of <50 μl) thereto and connection of appropriate lead wires. Automated dispensers for applying controlled amounts of sample to the electrode at the appropriate location are known and any such dispenser, or for that matter careful manual dispensing, may be used to contact the sample with the electrode. Specifically, dispensers of the type disclosed in U.S. Patent No. 3,572,400 may be adapted for applying small quantities (i.e., drops) to the surface of the electrode of the present invention. Other suitable dispensers are described in German Offenlegungsschrift 2,559,090. Alternatively, when wires, cylinders and rods, i.e., structures comprising other than planar surfaces which can be spotted, are used for the electrode, the electrode may actually be immersed in or contacted with the surface of the solution under analysis.

Second reference electrodes such as saturated calomel electrodes for use in combination with the integral electrodes of the present invention are also well known. In addition to such electrodes, reference elements of the type described herein as the internal references may also be used as the second or external reference electrode.

Similarly, potentiometers capable of reading the potentials generated in the ion-selective electrodes of the present invention are well known and, when properly connected as described hereinafter, can be used to give a sensory indication of the potential from which the ionic activity in the unknown solution may be calculated.

By incorporating computing capability into the potentiometric device it is, of course, possible, to obtain direct readings of specific ionic concentrations in solution as a function of ionic activity.

As referred to numerous times herein, it is in their use that the electrodes of the present invention demonstrate their highly unexpected properties. Thus, while many prior art electrodes require preconditioning, wet storage or an equilibration period prior to use, the electrodes of the present invention, apparently because of their *dried* internal reference electrodes and the predetermined uniform thickness of their ion-selective membrane can be used without any need for conventional preconditioning, wet storage or equilibration protocols.

It is now been discovered that, when electrodes of the type described herein are stored under ambient conditions of the type normally encountered in a

laboratory environment (most generally at or below RH about 65%) and subsequently spotted or otherwise contacted with samples of an aqueous ion-containing liquid as described above, under reproducible, known conditions, reproducible traces of the potential exhibited by these electrodes will define traces of potential vs. time as shown in Figure 3. The phenomenon which is represented by this curve shape is "drift" which is defined hereinafter.

The shape of the curve produced by any specific electrode is determined by its composition and configuration. As described above, it is theorized that drift, particularly in electrodes as described herein, is related primarily to the thickness and composition of the ion-selective membrane which regulates the rate of water permeation of the electrode. Thus, the composition and configuration (e.g., physical dimensions such as thickness of the electrode) play a very significant role in the trace defined by any specific electrode or set of electrodes. Specific results attained by varying such thicknesses are shown in Example 47. It should, therefore, be apparent that if precise measurements are to be achieved using a series of disposable, single-use electrodes, it is important that the thickness and composition of the ion-selective membrane be carefully controlled and maintained at some predetermined uniform thickness from electrode to electrode and within regions of a single electrode intended for contact with the test sample. A lack of such predetermined controlled thickness uniformity will manifest itself as random or erratic drift which cannot be calibrated as described herein. Such drift will render it difficult, if not impossible, to calibrate a series of electrodes because variations in membrane thickness from electrode to electrode result in calibration curves having different shapes which cannot be related to ion activity or concentration in any meaningful fashion.

A study of Figure 3 indicates that, after some appropriate interval, generally about 10 minutes, in electrode configurations of the type described herein, the potentials exhibited by the various electrodes begin to stabilize (i.e. the slope becomes constant) thus indicating the attainment of the intitial stages of equilibrium within the electrode. It is in the extremes of this stabilized portion of the potentiometric curve after wet storage or preconditioning that measurements of potential were made with the electrodes of the prior art and from which ion concentrations were calculated using the Nernst equation. It has been discovered that using the electrodes of the present invention after storage at ambient conditions, the drift can actually be calibrated and that, using "calibrated drift", ionic concentration is reproducibly and accurately determinable almost immediately after contact of the surface of the electrode with the aqueous test solution. Such results are achieved without according the electrode any specialized storage treatment prior to use except to insure freedom from contamination as would be done for conventional laboratory glassware and equipment.

The depth and width of the trough will vary somewhat depending upon the ambient condition of use (primarily the relative humidity) and the thickness of the various layers (principally the hydrophobic membrane); however, these variations are easily compensated for by using either a differential measurement which compares the ion concentration of the unknown sample with that of a similar sample of known ion concentration (i.e., a calibrator or standard) simultaneously applied to an identical electrode, or by initially deriving calibration curves for the electrode for given sets of ambient conditions and subsequently relating the conditions of individual measurements to such calibration curves.

As will be described in the examples below, when electrodes prepared as described in U.S. Patent No. 3,856,649 were stored "dry," i.e., at relative humidity below about 65%, and used as just described, a somewhat similar drift was observed; however, in these cases the drift was random and erratic, varied substantially from electrode to electrode and generally provided "uncalibratable" results, due most probably to the nonuniform thickness of the layers of such electrodes and the need for the reference electrode to be hydrated or equilibrated before true and uniform contact between the internal reference electrode and the hydrophobic membrane occurred.

Quite clearly, it is difficult to manufacture an electrode having layers of predetermined uniform thickness using a dipping technique, although such an electrode could conceivably be prepared using coating solutions of highly controlled viscosity and rotating the dipped work piece in a fashion which inhibits formation of a bulbous structure of non-uniform thickness. In view of the difficulties in use of such techniques, applicants prefer to prepare their electrodes in a planar format which not only simplifies manufacturing techniques but allows

use by simply depositing a very small quantity (i.e., micro amounts on the order of less than 50 μl) onto the planar electrode and measuring therefrom.

The following examples illustrate the manufacture and use of electrodes in including ion selective electrodes according to the present invention.

Example 1:
Ag/AgX Electrode—Method 1

A sample of vacuum-deposited metallic silver on polyethylene terephthalate support (~10 mg Ag/dm²) was prepared. A portion of this sample was treated for 5 minutes in the following solution:

glacial acetic acid	0.45 ml
sodium hydroxide	0.20 g
potassium ferricyanide	0.80 g
potassium bromide	2.50 g
distilled water to 1 litre	

The sample was then washed for 5 minutes in running distilled water.

Visual inspection revealed that partial conversion to silver bromide had occurred, leaving a contiguous layer of metallic silver adjacent the support. A narrow strip along one edge was dipped briefly in a thiosulphate bath to uncover the silver layer for purposes of making electrical contact.

Measurements of the electrochemical response were performed by applying small samples of aqueous solutions varying in Br⁻ activity to the silver bromide layer. A linear response, with approximately theoretical slope (Nerst equation), was observed.

Ag/AgX Electrode—Method 2

Alternatively a Ag/AgX half-cell can be prepared as described above except that the conversion conditions are 30 seconds in a solution containing 8.45 g/l of potassium chlorochromate.

Measurements of electrochemical response have been performed and showed linear potential response with varying Cl⁻ and Ag⁺ activity.

Laminated Ion-Selective Electrode

A silver-silver chloride film on polyethylene terephthalate was prepared as described in Method 2, 7.6 g/m² total silver with 15% conversion to AgCl (1.16 g/m²) and then coated with a 5% polyvinyl alcohol (PVA)—0.2 M potassium chloride solution (1.5 g KCl, 5.0 g PVA/m². After the PVA layer was dried by heating to 54.5°C for 10 minutes, a precast ion-selective membrane comprising 0.50 g/m² of valinomycin (VAL), 40.4 g/m² of polyvinyl chloride (PVC) and 100.2 g/m² of bromophenyl phenyl ether (BPPE) as carrier solvent was manually laminated on top of the film coating.

The resulting ion-sensitive electrode, represented as Ag/AgCl/PVA-KCl/ion-selective membrane was tested by:

(1) connecting the silver-silver chloride film to the high-impedance input of a volt meter; and

(2) suspending a drop (25—50 μl) of the potassium chloride solution to be measured from the tip of a saturated sodium nitrate salt bridge which was connected to an external reference electrode (Hg/Hg₂Cl₂) which was in turn connected to the reference input of the volt meter, and contacting the drop to the surface of the electrode. The complete potentiometric cell is represented by:

Hg/Hg₂Cl₂/KCl(XM) test/ion-selective membrane, PVA-KCl/AgCl/Ag.

A linear semilogarithmic response to potassium ion concentration was observed with a slope of 57 mv/decade over the range pK⁺ 1 to 4.

Example 2:
Coated Ion-Selective Electrode

An electrode was prepared as in Example 1 except that the ion-selective membrane comprising 0.58 g/m² VAL, 22.9 g/m² polyvinyl chloride and 111.2 g/m² BPPE was coated directly on the KCl-PVA layer rather than being laminated as in Example 1.

This integral electrode was tested as in Example 1 and exhibited a linear semilogarithmic response to potassium ion concentration having a slope of 55 mv/decade.

Example 3:
Reference Electrolyte Composition Variations

A series of electrodes were prepared using a variety of surfactants and water-soluble polymers as binders for potassium chloride in the reference electrolyte solution. The polymers included polyvinyl alcohol (PVA), deionized gelatin and polyacrylamine (PAM) (see Table 1). Unless otherwise noted, all electrodes contained 1.5 g/m² KCl. These electrodes were then laminated with a precast ion-selective membrane of the composition described in Example 1. The resulting electrodes were then evaluated as described in Example 1, with the results shown in Table 1 below.

TABLE 1
Internal Reference Element Binder Variations

Test #	Binder	Spreading Agent g/m²	Response mv/decade	Range
1	PVA	—	56	$10^{-4} \to 10^{-1} M\ K^+$
2	PVA	—	55	$10^{-4} \to 10^{-1} M\ K^+$
3	PVA	3.0 10G*	53	$10^{-4} \to 10^{-1} M\ K^+$
4	PVA	4.6 Saponin	57	$10^{-4} \to 10^{-1} M\ K^+$
5	gelatin	0.02 PEG**	51	$10^{-4} \to 10^{-1} M\ K^+$
6	PAM	0.02 PEG**	53	$10^{-4} \to 10^{-1} M\ K^+$

*"Surfactant" 10G is a nonyl phenyl polyglycidol commercially available from Olin-Mathieson, N.Y.
**Polyethylene Glycol

The data of Table 1 demonstrate that the electrodes prepared as described give a linear response to potassium ion concentration with a slope between 51 and 57 mv/decade.

Examples 4 to 14:
Ion-Selective Membrane Composition

A number of electrodes, both laminated and coated, were prepared to examine the effect of variations in the composition of the ion-selective membrane on the response of the electrode.

The elements were evaluated as described in Example 1 with the results shown in Table 2 below.

TABLE 2
Valinomycin—PVC—BPPE Variations

Fixed Components of Coated Electrodes
7.6 g/m² Total Ag—1.16 g/m² AgCl, 5.0 g/m² PVA, 0.82 g/m² KCl

	VAL	g/m² PVC	BPPE	Response mv/decade	Range
4	0.1	5	5	none	—
5	0.1	5	10	none	—
6	0.1	10	10	poor	—
7	0.5	10	20	poor	—
8	0.5	15	40	57	$10^{-4} \to 10^{-1} M\ K^+$

Fixed Components of Laminated Electrodes
7.6 g/m² Total Ag—1.16 g/m² AgCl, 5.0 g/m² PVA, 1.49 g/m²KCl

	VAL	g/m² PVC	BPPE	Response mv/decade	Range
9	0.5	10	10	none	—
10	0.5	10	20	48	$10^{-4} \to 10^{-1} M\ K^+$
11	0.5	10	40	57	$10^{-3} \to 10^{-1} M\ K^+$
12	0.5	10	25	51	$10^{-4} \to 10^{-1} M\ K^+$
13	0.2	40	80	45	$10^{-4} \to 10^{-1} M\ K^+$
14	0.1	40	80	nonlinear	

The data in Table 2 illustrate the following effects as a function of variations of VAL, BPPE and PVC in the electrode format:

A. Less than 0.2 g/m² of valinomycin in the membrane results in either marginal or no potassium ion response.

B. BPPE/PVC ratios of less than 1:1 give dry unresponsive membranes. In general, carrier-solvent-to-polymer ratios of between 1:1 to 5:2 provide useful membrane layers.

Examples 15 to 20:
Ion-Selective Membrane Composition

A number of electrodes, both laminated and coated, were prepared to demonstrate the utility of other polymers in the ion-selective membrane layer of the electrode. Polymers which were tested include "Butvar" B76 (the registered Trade Mark of a polyvinyl butyral available from Monsanto Chemical Co.), "Estane" 510F1 (the registered Trade Mark of an aromatic polyurethane available from B. F. Goodrich), "VYNS" (a PVC/PVA$_c$*—90/10 copolymer available from Union Carbide) and "Silastic" 731RTV (the registered Trade Mark of a silicone rubber available from Dow Corning, Midland, Michigan). After preparation, the electrodes were evaluated as described in Example 1, with the results shown in Table 3 below.

*PVA$_c$=polyvinyl acetate

TABLE 3
Polymer Variations

Fixed Components

7.6 g/m² Total Ag, 1.16 g/m² AgCl, 5.0 g/m² PVA, 1.5 g/m² KCl

Test #	VAL	g/m² Polymer	BPPE	mv/dec Response	Range
15	0.5	10 PVC	25	51	$10^{-4} \rightarrow 10^{-1}$M K$^+$
16	0.5	10 VYNS	25	42	$10^{-4} \rightarrow 10^{-1}$M K$^+$
Laminated					
17	0.5	40 "Estane"	80	58	$10^{-4} \rightarrow 10^{-1}$M K$^+$
18	0.5	40 (1:1, "Estane" 5107Fl: PVC)	80	58	$10^{-4} \rightarrow 10^{-1}$M K$^+$
19	0.5	40 PVC	100	55	$10^{-4} \rightarrow 10^{-1}$M K$^+$
Coated or Laminated					
20	3.1	116 RTV "Silastic"	100	56	$10^{-4} \rightarrow 10^{-1}$M K$^+$

The data of Table 3 illustrate that all of the polymers tested are useful in the present electrode configuration.

Examples 21 to 34
Ion-Selective Membrane Composition
(Carrier-Solvents)

A series of electrodes were prepared to compare bromophenyl phenyl ether (BPPE) with other possible carrier solvents for the membrane layer. The other solvents which were tested include the following: 3-methoxyphenyl phenyl ether (3 MPPE), 4-methoxyphenyl phenyl ether (4MPPE), dimethylphthalate (DMP), dibutylphthalate (DBP), dioctylphenylphosphonate (DOPP) and bis(2-ethylhexyl)phthalate (BEHP) and dibutyl sebacate (DBS).

The integral electrodes were evaluated in the manner described in Example 1 with the results shown in Table 4 below.

1,584,788

TABLE 4
Carrier-Solvent Variations

Test #	VAL	g/m² PVC	Solvent	mv/dec Response	Range
Laminated Electrodes					
7.6 g/m² Total Ag, 1.16 g/m² AgCl, 5.0 g/m² PVa, 1.5 g/m² KCl					
21	0.5	40	60 4MPPE	55	$10^{-4} \to 10^{-1}$M K$^+$
22	0.5	40	70 4MPPE	50	$10^{-4} \to 10^{-1}$M K$^+$
23	0.5	40	80 4MPPE	56	$10^{-4} \to 10^{-1}$M K$^+$
24	0.5	40	90 4MPPE	52	$10^{-4} \to 10^{-1}$M K$^+$
25	0.5	40	80 3MPPE	52	$10^{-4} \to 10^{-1}$M K$^+$
26	0.5	40	100 BPPE	55	$10^{-4} \to 10^{-1}$M K$^+$
Laminated Electrodes					
3.4 g/m² Total Ag, 0.76 g/m² AgCl, 5.0 g/m² PVA, 1.5 g/m² KCl					
27	0.5	40	100 DMP	33	$10^{-4} \to 10^{-1}$M K$^+$
28	0.5	40	100 DBP	49	$10^{-4} \to 10^{-1}$M K$^+$
29	0.5	40	100 BPPE	55	$10^{-4} \to 10^{-1}$M K$^+$
Coated Electrodes					
7.6 g/m² Total Ag, 1.16 g/m² AgCl, 5.0 g/m² PVA, 1.5 g/m² KCl					
30	0.5	10	25 BPPE	51	$10^{-4} \to 10^{-1}$M K$^+$
31	0.5	10	25 MPPE	50	$10^{-4} \to 10^{-1}$M K$^+$
32	0.5	10	25 MPPE	55	10^{-1}M K$^+$
Coated Electrodes					
6.6 g/m² Total Ag—0.44 g/m² AgCl, 4.84 g/m² PVA, 1.45 g/m² KCl, 0.1 g/m² Triton X-100 (octylphenoxy polyethoxy ethanol, commercially available from Rohm and Haas Co.)					
33	0.5	10	25 DBS	52	$10^{-4} \to 10^{-1}$M K$^+$
34	0.5	10	25 BEHP	57	$10^{-4} \to 10^{-1}$M K$^+$

The data in Table 4 illustrate that the use of the phenyl ethers, phthalates and the sebacate as carrier-solvents results in electrodes which give good potassium ion response.

Example 35:

Electrodes were prepared and evaluated as described in Example 1 using various combinations of carrier solvent and coating solvents in the membrane layer. The results are shown in Table 5.

BEHP=Bis ethylhexyl phthalate
THF=tetrahydrofuran
MEK=methyl ethyl ketone
DDP=didodecyl phthalate

The composition of the membranes were as follows:

0.48 g/m² valinomycin
9.76 g/m² polyvinylchoride
0.15 g/m² carrier-solvent

TABLE 5

Carrier Solvent	Coating Solvent	Slope (Range of Multiple Measurements) millivolts per decade
BEHP	THF	51.9—59.3
BEHP	MEK	56.3—58.9
DDP	THF	56.2—59.3
DDP	MEK	53.5—58.6

Example 36:
Electrode Sensitivity

A coated electrode was prepared as described in Example 1 and tested for selectivity as described below.

Composition
6.9 g/m² Total Ag
1.4 g/m² AgCl
1.5 g/m² KCl
5.0 g/m² PVA
9.68 g/m² PVC
24.2 g/m² DDP
0.48 g/m² VAL

Evaluation:

The normal level for potassium ion in blood serum is 4 meq/litre while that for sodium is 30 to 40 times higher It is important, therefore, that sodium ion not interfere with the potassium ion measurement to any substantial degree. To examine the extent to which sodium ion interferes with the potassium ion response, the selectivity coefficient $K_K{}^+/_{Na+}$, defined by the equation:

$$E=E°+2.303\frac{RT}{F}\log[(a_{K+}+(K_{K+}/_{Na+})a_{Na+})]$$

was determined for the above-described coating. Measurements on this coating, using the constant interferent method gave a value of 1×10^{-3} in 0.15 M NaCl. In a solution containing 5 mM K^+ and 150 mM Na^+, the sodium response exhibited by this coating represents about a 3% interference. Thus, small variations in Na^+ over the clinical range, i.e., 0.12 M to 0.16 M Na^+ result in less than 1% variation in the interference.

Example 37:

A redox reference electrode having a double-layer structure was prepared by coating poly(ethylene terephthalate) film support with a conductive layer comprising gelatin (9.7 g/m²), particulate carbon (15.5 g/m²) and "Triton" X-100 (the registered Trade Mark of a polyethoxy ethanol surfactant commercially available from Rohm & Haas Co.) (0.28 g/m²) and a redox layer comprising deionized gelatin (4.85 g/m²) as a binder, potassium ferricyanide (5.4 meq/m²), and potassium ferrocyanide (5.4 meq/me²). The resulting reference electrode was manually laminated to a precast ion-selective membrane comprising valinomycin (VAL) (0.49 g/m²), bis(2-ethylhexyl)phthalate (BEHP) (14.5 g/m² and polyvinyl chloride (PVC) (9.2 g/m²).

The resulting composite ion-selective electrode was tested in the following cell:

0.15M	50λ drop of 0.1	5M ion-selective
NaCl CE	NaCl containing 10^{-1} to 10^{-4} KCl	electrode

TABLE 6
Potassium Ion Response
Fe(II)/Fe(III) Internal Reference

KCL M	2 Min. (mv)
10^{-4}	−59.0
10^{-3}	−3.7
10^{-2}	+54.4
10^{-1}	+108.2

The emf at 2 minutes shows a linear semilogarithmic dependence on potassium ion concentration with a slope of 57 mv/decade. The potential drifts with time after spotting the element with 50 ml of test solution. The magnitude of the reproducible drift is about 0.1 mv/minute between 2 and 10 minutes.

Example 38:
Ion-Selective Electrode Utilizing Single-Layer
Fe(II)/Fe(III) Reference Electrode

A reference electrode having a single-layer structure was prepared by coating polyethylene terephthalate film support with a layer comprising deionized gelatin as binder (4.3 g/m²), particulate carbon (6.9 g/m²), octylphenoxy polyethoxy

ethanol (0.12 g/m^2), potassium ferricyanide (7.5 meq/m^2) and potassium ferrocyanide (7.5 meq/m^2). The resulting reference electrode was then manually laminated to a precast ion-selective membrane comprising valinomycin (0.49 g/m^2), BEHP (14.5 g/m^2) and PVC (9.2 g/m^2).

The resulting integral electrode was evaluated in the manner described in Example 36 with the following results:

TABLE 7
Potassium Ion Response of Integral Electrode
Having "Single-Layer" Fe(II)/Fe(III)

KCL M	2 Min (mv)
10^{-4}	−64.0
10^{-3}	−5.8
10^{-2}	+49.6
10^{-1}	+102.4

The emf at 2 minutes shows a linear semilogarithmic dependence on potassium ion concentration with a slope of 55 mv/decade. The potential of this "single-layer" format drifts at a rate of about 1.0 mv/minute between 2 and 10 minutes.

Example 39:
Electrode Utilizing Double Layer Co(II)/Co(III) Reference Electrode

A reference electrode having a double-layer structure was prepared by coating polyethylene terephthalate film support with a conductive layer comprising deionized gelatin as binder (9.8 g/m^2), particulate carbon (15.6 g/m^2), saponin (0.2 g/m^2) and bis(vinylsulphonylmethyl)ether (0.1 g/m^2) followed by a redox layer comprising deionized gelatin (10.8 g/m^2) octylphenoxy polyethoxy ethanol (0.22 g/m^2), bis(vinylsulphonylmethyl)ether (0.22 g/m^2), Co(terpyridyl)$_2$(BF$_4$)$_2$ (210 μmoles/m^2). The resulting coating was then soaked for 30 minutes in 0.1 N KCl, dried in room air for 24 hours and then manually laminated to a precast ion-selective membrane comprising VAL (0.49 g/m^2) BEHP (14.5 g/m^2) and PVC (9.2 g/m^2).

The bathing step in the preparation procedure was included in this example as a method of absorbing potassium ion into the redox layer to poise the potential of the membrane. This step was not necessary in Examples 36 and 37 because the ferro/ferricyanide buffer was prepared with potassium salts.

The evaluation of the element was carried out as in Example 36 with the following results:

Table 8
Potassium Ion Response of Integral
Electrode Having "Double-Layer"
Co(II)/Co(III) Internal Reference

KCL M	Cell Emf at 2 Min. (mv)
10^{-4}	−237.4
10^{-3}	−183.2
10^{-2}	−126.3
10^{-1}	−68.5

The emf at 2 minutes shows a linear semilogarithmic dependence on potassium ion concentration with a slope of 57 mv/decade. The potential drifts at a rate of about 0.1 mv/minute over 3 to 10 minutes.

Example 40:
Coated electrodes were prepared as described in Example 2, but with the following compositions for the reference electrolyte layer and the ion-selective membrane:

Reference Electrolyte Layer	PVA	4.8 g/m^2
	KCl	~2.4 g/m^2
Ion-Selective Membrane	PVC	9.7 g/m^2
	DDP	14.6 g/m^2
	Valinomycin	0.5 g/m^2

Figure 3 shows the shape of E vs. Time curves obtained by varying the thickness of the foregoing layers by doubling the laydown of the respective compositions. As is clear these curves have different shapes, however, each is calibratable and can provide precise and accurate indications of potential related to ion activity and concentration.

Example 41:

Coated electrodes were prepared as described in Example 2, but with the following compositions for the reference electrolyte layer and the ion-selective membrane:

Reference Electrolyte Layer

Gelatin	5 g/m^2
Sodium chloride	2.5 g/m^2
Surfactant	.09 g/m^2

Ion-Selective Membrane

PVC (1.8% carboxylated)	10 g/m^2
Tris(2-ethylhexyl)phosphate	12.5 g/m^2
Sodium Tetraphenyl Boron	.6 g/m^2
Surfactant	.06 g/m^2

When drop size samples of aqueous sodium ion solutions were applied to this electrode a Nernstian slope of 57 mv/dec was observed.

Example 42:

Coated electrodes were prepared as described in Example 34, but with the following composition for the ion-selective membrane:

Ion-Selective Membrane

PVC	10 g/m^2
4-octyltrifluoroacetophenone	5 g/m^2
Didodecylphthalate	10 g/m^2
Trioctylpropylammonium Chloride	.5 g/m^2

This electrode demonstrated a slope of 27 mv/dec when an aqueous sample containing $CO_3^=$ was applied to the ion-selective membrane.

Example 43:

Coated electrodes were prepared as described in Example 34, but with the following composition for the ion-selective membrane:

Ion-Selective Membrane

PVC	10 g/m^2
Didodecyldimethylammonium Chloride	15 g/m^2
Didodecylphthalate	.25 g/m^2
Trioctylpropylammonium Chloride	.25 g/m^2

This electrode demonstrated a Nernstian slope of 58 mv/dec when contacted with aqueous solutions containing chloride ion.

Although the multilayer electrode elements of the present invention have been described primarily in connection with the potentiometric quantitation of alkali metal and alkaline earth ions, the structures, compositions and techniques described herein are equally applicable to the assembly of electrodes for the analysis of other cations such as NH_4^+ and anions such as $SO_3^=$ principally by the selection of appropriate ion-specific carriers for the ion-selective membrane, and such electrodes are clearly within the contemplated scope of the instant invention.

Furthermore, it is within the scope of the instant invention to incorporate protective overlayers for the electrode which may serve merely to protect the surface thereof, increase mechanical strength, or serve multiple additional purposes such as permitting selective permeability to a specific ion, or permeability only to a particular gaseous component of a solution under test, for example, oxygen or carbon dioxide.

It is also contemplated that electrodes of the type described herein would be useful in combination with overlayers containing enzymes which act upon a

substrate specifically and selectively to release ions which can be quantified by the electrode.

WHAT WE CLAIM IS:—

1. An ion-selective electrode comprising an internal reference electrode in dried form as herein defined, in contact with a hydrophobic dry-operative, as herein defined, ion selective membrane containing a binder and an ion-carrier, the regions of the membrane adapted to be in contact with analyte having a predetermined uniform thickness.

2. An ion-selective electrode as claimed in claim 1 in which the reference electrode includes a supported electrically conducting layer.

3. An ion-selective electrode as claimed in claim 2 in which the support is cellulose acetate, poly(ethylene terephthalate), polycarbonate or polystyrene.

4. An ion-selective electrode as claimed in any of the preceding claims in which the reference electrode is a metal/metal salt electrode comprising an electrically conducting layer of a metal in contact with a layer of an insoluble salt of the metal.

5. An ion-selective electrode as claimed in claim 4 in which the metal is silver and the insoluble salt is a silver halide.

6. An ion-selective electrode as claimed in claim 4 in which the insoluble salt is silver chloride.

7. An ion-selective electrode as claimed in any of the claims 4 to 6 in which the electrode is in contact with a dried electrolyte layer comprising a hydrophilic matrix containing a water soluble salt having the same anion as the insoluble salt of the metal.

8. An ion-selective electrode as claimed in claim 7 in which the hydrophilic matrix is polyvinyl alcohol, gelatin, agarose, polyacrylamide, polyvinyl pyrrolidone, polyhydroxyethyl methacrylate, poly(hydroxyethyl acrylate) or polyacrylic acid.

9. An ion-selective electrode as claimed in any of the preceding claims in which the hydrophobic dry-operative ion selective membrane contains polyvinyl chloride, a polyurethane, a carboxylated polyvinyl chloride, a copolymer of vinyl chloride and vinyl acetate, a silicone elastomer, a polycarbonate, a cellulose ester, a copolymer of vinyl choride and vinylidene chloride, a polyvinyl butyral or a polyvinyl formed as a binder.

10. An ion-selective electrode as claimed in any of the preceding claims in which the ion-carrier in the ion-selective membrane is valinomycin, a cyclic polyether, tetrophenyl borate, a tetralactone, a macrolide acetone, a cyclic polypeptide, a quaternary ammonium salt, a compound having the formula:

$$
\begin{array}{c}
R^2 \diagdown \diagup R^1 \\
N \\
| \\
C \diagup\!\!\diagdown O \\
| \\
CH_2 \\
| \\
O \\
| \\
CH_2 \\
| \\
CH_2 \\
| \\
O \\
| \\
CH_2 \diagdown \diagup O \\
C \\
| \\
N \\
\diagup \diagdown \\
R^2 \quad R^1
\end{array}
$$

wherein:

I R^1 is —CH_3 and R^2 is —(CH_2)—$_n COO$—CH_2CH_3 and n is 1 to 10

II R^1 is —CH_3 and R^2 is —$(CH_2)_6$—CH_3

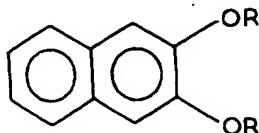III R^1 and R^2 are each —$CH_2CH_2CH_3$

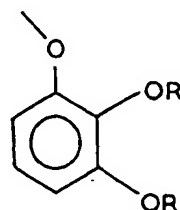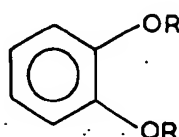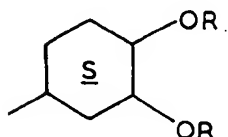IV R^1 is —$CH_2CH_2CH_3$ and R^2 is —CH_2—C—$(CH_3)_3$

V R^1 and R^2 are each phenyl groups

or

VII R^1 and R^2 are each benzyl groups or a compound having a formula:

cis and trans

or

wherein R is

$$-CH_2CON(CH_2CH_2CH_3)_2$$

$$\text{or } -CH_2-CON-(-CH_2-)_{11}-CO_2CH_2CH_3.$$
$$\underset{CH_3}{|}$$

11. An ion-selective electrode as claimed in any of the preceding claims in which the ion-selective membrane contains a solvent for the ion carrier.

12. An ion-selective electrode as claimed in claim 11 in which the ion carrier solvent is an aromatic ether, an aliphatic ether, a phthalate, an adipate, a sebacate or phosphate.

13. An ion-selective electrode as claimed in claims 11 or 12 in which the ratio of ion carrier solvent to binder in the ion-selective membrane lies in the range from 1:1 to 5:2 by weight.

14. An ion-selective electrode as claimed in claims 1 to 3 in which the reference electrode is a redox internal reference electrode comprising an electrically conducting layer in contact with a redox couple capable of electrochemical contact upon wetting the electrode.

15. An ion-selective electrode as claimed in claim 14 in which the electrically conducting layer comprises carbon, platinum, gold or nickel.

16. An ion-selective electrode as claimed in claim 15 in which the electrically conducting layer comprises particulate carbon in a binder.

17. An ion-selective electrode as claimed in claim 16 in which the binder is gelatin, polyvinyl alcohol, polyacrylic acid or poly(vinyl pyrrolidone).

18. An ion-selective electrode as claimed in any of the claims 14 to 17 in which the redox couple consists of a material a portion of which is in a first oxidation state and a portion of which is in a second oxidation state.

19. An ion-selective electrode as claimed in claim 18 in which the two components of the redox couple are present in a molar ratio of 1 to 1.

20. An ion-selective electrode as claimed in claims 18 and 19 in which the redox couple comprises ferricyanide and ferrocyanide ions or cobaltic and cobaltous terpyridyl ions.

21. An ion-selective electrode as claimed in any of the claims 14 to 20 in which the hydrophobic dry-operative ion selective membrane contains polyvinyl chloride,
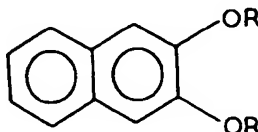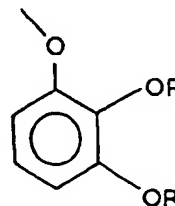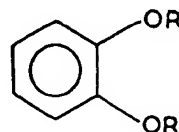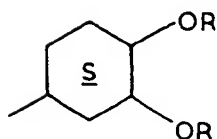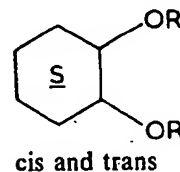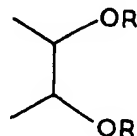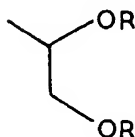
a copolymer of vinyl chloride and vinyl acetate, a silicone elastomer, a polycarbonate or a cellulose ester as a binder.

22. An ion-selective electrode as claimed in claims 14 to 21 in which the ion-carrier in the ion-permeable membrane is valinomycin, a cyclic polyether, tetraphenyl borate, a tetralactone, a macrolide acetone, a cyclic polypeptide, a quaternary ammonium salt, a compound having the formula:
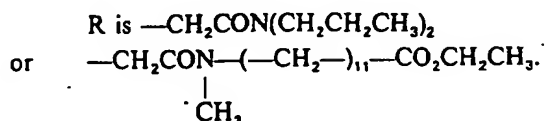

wherein:
I R^1 is —CH$_3$ and R^2 is —(—CH$_2$—)$_n$—COO—CH$_2$CH$_3$ and n is 1 to 10
II R^1 is —CH$_3$ and R^2 is —(CH$_2$)$_6$—CH$_3$
III R^1 and R^2 are each —CH$_2$CH$_2$CH$_3$
IV R^1 is —CH$_2$CH$_2$CH$_3$ and R^2 is —CH$_2$—C—(CH$_3$)$_3$
V R^1 and R^2 are each phenyl groups, or
VII R^1 and R^2 are each benzyl groups or a compound having a formula:

cis and trans

or

wherein

R is —CH$_2$CON(CH$_2$CH$_2$CH$_3$)$_2$
or   —CH$_2$CON—(—CH$_2$—)$_{11}$—CO$_2$CH$_2$CH$_3$.
              |
             CH$_3$

1,584,788

23. An ion-selective electrode as claimed in claims 14 to 22 in which the ion-selective membrane contains a solvent for the ion-carrier.

24. An ion-selective electrode as claimed in claim 23 in which the ion carrier solvent is an aromatic ether, an aliphatic ether, phthalate, or a sebacate.

25. An ion-selective electrode as claimed in claim 23 or 24 in which the ratio of ion carrier solvent to binder in the ion-selective membrane lies in the range from 1:1 to 5:2 by weight.

26. An ion-selective electrode as claimed in claim 1 and as herein described.

27. An ion activity measuring device comprising a frame carrying a pair of electrodes, at least one of which is an ion-selective electrode as claimed in any of the claims 1 to 26, and means for accepting drops of analyte and providing ionic flow between the electrodes.

28. A device as claimed in claim 27 in which the ionic flow providing means includes a porous layer extending between the electrodes.

29. A device as claimed in claim 28 in which the porous layer comprises a binder, thickener and a polycarbonate or polyamide polymer.

30. A device as claimed in any of the preceding claims in which both electrodes are the same and are ion-selective electrodes as claimed in any of the claims 1 to 26.

31. A device as claimed in claim 30 in which the flow-providing means includes transport means for promoting migration between two drops of liquid having different ionic strength so that one drop is in contact with each electrode and the drops form an ionic junction.

32. A device as claimed in claim 31 which includes a hydroscopic gel saturated with an ionically conductive salt for minimizing the potential at the ionic junction.

33. A device as claimed in claim 31 in which the transport means includes a passageway in the frame extending between the electrodes.

34. A device as claimed in claim 33 in which the passageway contains a fibrous material.

35. A device as claimed in any of the claims 30 to 34 in which the frame includes a pair of cavities containing the electrodes and at least one aperture adjacent and connected to each of the cavities and to the surface of the frame to permit access to the electrodes.

36. A device as claimed in any of the claims 27 to 29 in which one electrode is a reference electrode and the other an ion-selective electrode as claimed in any of the claims 1 to 26.

37. A device as claimed in claim 36 in which the flow-providing means includes restraining means for ensuring that drops of analyte only contact the surface of the electrodes.

38. A device as claimed in claim 37 in which the restraining means comprises a platform adjacent and spaced away from each of the electrodes and an annular groove separating the platform from the rest of the frame, the groove having a geometry and dimensions which are sufficient to confine the drop to that portion of each electrode which is adjacent to the platform.

39. A device as claimed in claim 38 in which the frame has a pair of cavities, the electrodes being fixedly mounted within the cavities, and at least one aperture adjacent and connected to each of the cavities and to one surface of the frame to permit access to the cavities.

40. A device as claimed in claim 39 in which the flow-providing means includes a hinge positioned between the apertures such that, when the frame is folded about the hinge, the apertures are aligned and a single drop of solution can contact the surface of both electrodes.

41. A device as claimed in claim 40 in which the frame includes additional apertures extending from one surface into either of the cavities, such that, when the frame is folded about the hinges, the additional apertures are aligned with the rear of the electrodes to permit electrical contact with the electrode.

42. Ion activating measuring devices as claimed in claim 27 and as herein described.

43. A method of determining the specific ion activity of an aqueous liquid comprising applying a sample of the aqueous liquid to the ion-selective membrane of an electrode, as claimed in any of the claims 1 to 26, and measuring the electrical potential shown by the electrode before equilibrium is reached.

44. The method as claimed in claim 43 wherein the electrode is planar and the sample of aqueous liquid is less than 50 microlitres.

45. Methods of determining specific ion activity as claimed in claim 43 and as herein described.

46. A method of forming an ion-selective electrode as claimed in any of the claims 1 to 26 comprising forming the reference electrode, drying the electrode and thereafter forming the hydrophobic ion-selective membrane over the dry electrode.

47. The method as claimed in claim 46 in which the ion-selective membrane is laminated to the dry surface of the electrode.

48. Methods of forming ion-selective electrodes as claimed in claim 46 and as herein described.

L. A. TRANGMAR, B.Sc., C.P.A.,
Agent for the Applicants.

Fig.1

Fig.2

FIG.3